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ning of each regular issue of the PCT Gazette.*

(54) Title: METHODS FOR THE IDENTIFICATION OF AGENTS THAT MODULATE THE STRUCTURE AND PROCESSING OF BETA-AMYLOID PRECURSOR PROTEIN

(57) Abstract: The present invention provides methods for the screening and identification of agents from a large library of molecular structures that can alter the cleavage of amyloid precursor protein (AP). Agents identified by the methods of the present invention that modify the cleavage of APP can be used in the treatment and prevention of Alzheimer's disease. The methods select for and identify effector agents that bind to APP causing a structural change in the structure of APP in such a way that the efficiency of the cleavage of a secretase is modulated. Further, the methods are carried out in an in vivo system that provides for physiological conditions similar or identical to conditions for APP processing. Agents can be selected for their ability to cause a decrease in the amount of B-secretase or γ -secretase cleavage of APP, or for an increase in a-secretase cleavage of APP. The agents can be, particularly peptide agents, can be converted into a peptidomimetic, an isosteric replacement compound, a D-amino acid analog, or non-peptidyl compound for treating Alzheimer's disease or any other amyloid related or prion related disease. The agents or derivatives thereof can be formulated for intravenous, parenteral, topical, sustained release, intranasal, or inhalation use.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/35294

A. CLASSIFICATION OF SUBJECT MATTER IPC(7) : C12N 15/00; G01N 33/53, 33/567; A61K 49/00 US CL : 435/7.1, 7.21, 172.3; 530/350; 800/3 According to International Patent Classification (IPC) or to both national classification and IPC																						
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) U.S. : 435/7.1, 7.21, 172.3; 530/350; 800/3 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EAST, MEDLINE																						
C. DOCUMENTS CONSIDERED TO BE RELEVANT <table border="1"> <thead> <tr> <th>Category *</th> <th>Citation of document, with indication, where appropriate, of the relevant passages</th> <th>Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td>X — Y</td> <td>US 6,440,698 B1 (GURNEY et al) 27 August 2002 (27.08.2002), column 10, lines 30-59; column 7, lines 34-46; column 35, line 7 to column 36, line 21.</td> <td>1-7, 36-38, 46 ----- 15-35, 39-45, 53-61</td> </tr> <tr> <td>X — Y</td> <td>US 6,175,057 B1 (MUCKE et al) 16 January 2001 (16.01.2001), column 16, lines 1-58; column 19, lines 35-39; column 16, lines 31-33; column 12, line 6 to column 13, line 61; column 17, lines 1-16.</td> <td>1, 8-14, 63 ----- 42-45, 49-50, 59-60</td> </tr> <tr> <td>X — Y</td> <td>US 5,604,102 A (MCCONLOGUE et al) 18 February 1997 (18.02.1997), column 9, line 16 to column 11, line 14; column 11, lines 28-42.</td> <td>1, 47-48, 51-52, 62 ----- 49-50</td> </tr> <tr> <td>Y</td> <td>US 2002/0127564 A1 (NOLAN) 12 September 2002 (12.09.2002), entire document, especially page 2, paragraph 25 and 27; page 3, paragraphs 37-38; page 4, paragraphs 41-45; page 5, paragraphs 51-53; page 11, paragraphs 105-107.</td> <td>15-20, 22-35, 50, 53-56, 58</td> </tr> </tbody> </table>			Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	X — Y	US 6,440,698 B1 (GURNEY et al) 27 August 2002 (27.08.2002), column 10, lines 30-59; column 7, lines 34-46; column 35, line 7 to column 36, line 21.	1-7, 36-38, 46 ----- 15-35, 39-45, 53-61	X — Y	US 6,175,057 B1 (MUCKE et al) 16 January 2001 (16.01.2001), column 16, lines 1-58; column 19, lines 35-39; column 16, lines 31-33; column 12, line 6 to column 13, line 61; column 17, lines 1-16.	1, 8-14, 63 ----- 42-45, 49-50, 59-60	X — Y	US 5,604,102 A (MCCONLOGUE et al) 18 February 1997 (18.02.1997), column 9, line 16 to column 11, line 14; column 11, lines 28-42.	1, 47-48, 51-52, 62 ----- 49-50	Y	US 2002/0127564 A1 (NOLAN) 12 September 2002 (12.09.2002), entire document, especially page 2, paragraph 25 and 27; page 3, paragraphs 37-38; page 4, paragraphs 41-45; page 5, paragraphs 51-53; page 11, paragraphs 105-107.	15-20, 22-35, 50, 53-56, 58					
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INTERNATIONAL SEARCH REPORT

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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Y	US 6,420,110 B1 (GYURIS et al) 16 July 2002 (16.07.02) entire document, especially column 2, lines 31-33; column 19, lines 22-29; column 43, lines 22-24; column 18, lines 11-29; column 9, lines 36-37; column 3, lines 35-37.	21, 24, 28, 32, 45, 58, 61
Y	RIAN, E et al. A Signal Sequence Trap Based on Cell Enrichment Using Anti-CD19 Antibody Coated Magnetic Beads. Scand. J. Immunol. September 2001, Vol. 54, pages 280-284, entire document.	26
Y	PONCET, C. CD24, a glycosphosphatidylinositol-anchored molecule is transiently expressed during the development of human central nervous system and is a marker of human neural cell lineage tumors. Acta Neuropathol. 1996, Vol. 91, No. 4, Abstract only.	30
Y	MURTHY, S.C. Characterization of the interleukin 3 receptor. Exp. Hematol. January 1990, Vol. 18, No. 1, Abstract only.	31
Y	MAZUR-KOLECKA, B. et al. Accumulation of Alzheimer amyloid-peptide in cultured myocytes is enhanced by serum and reduced by cerebrospinal fluid. J Neuropathol Exp Neurol. March 1997, Vol. 56, No. 3, Abstract only.	39-41, 57, 60